

Modeling the Dynamic Digestive System Microbiome [†]

Anne M. Estes

Institute for Genome Sciences, University of Maryland School of Medicine, Baltimore, MD 21201

INTRODUCTION

This exercise helps students understand the dynamics of microbiome ecology by modeling disturbance events in the human digestive system microbiome. Specifically, this exercise illustrates how microbiome diversity is influenced by: I) niche availability and habitat space and 2) major disturbance events, such as antibiotic use. Students will examine prepared models of digestive system microbiomes, model a disturbance event, and determine how resilient their model microbiome community is to disturbance and colonization from environmental microbes.

An initial activity focused on microbial diversity and antibiotic usage is described. Suggestions for extending and modifying the exercise to include diet changes and the emergence of antibiotic resistance are included. The digestive system microbiome activity is geared toward high school and introductory college students and could be used in the lecture or laboratory classroom.

PROCEDURE

Preparing students for the activity

An analogy for understanding the human microbiome. There are over 100 trillion microbes that live in or on the human body. We provide a variety of places for them to live and are their environment. Thus, from a microbial perspective, each individual person can be thought of as a planet composed of different ecosystems and habitats. Macroecology examples are useful for helping students make the transition from seeing themselves as individuals to thinking of themselves as a series of microbial ecosystems and habitats or a "microbial planet."

To discuss people as "microbial planets," have students identify abiotic and biotic characteristics of ecosystems on Earth. Temperature, moisture, pH, oxygen levels, and nutrients are a few physical parameters that may be easy

Corresponding author. Mailing address: Institute for Genome Sciences, University of Maryland School of Medicine, 801 W. Baltimore Street, BioPark II, Baltimore, MD 21201. Phone: 410-706-0790. E-mail: anneestes@gmail.com.

†Supplemental materials available at http://jmbe.asm.org

to discuss. Next, have students describe particular Earthly habitats specific to given organisms. Ask students to identify different ecosystems on their own bodies and list the physical characteristics of these potential microbial habitats.

The analogy of humans as "microbial planets" can then be extended to disturbance events. Ask students to identify major, catastrophic events that may change an environment and affect the organisms living within that habitat. Have students discuss how the habitats recover from these major events. Are the original organisms remaining? What happens if a population of a given organism is removed by the disturbance event?

Activity

"Modeling the Dynamic Digestive System Microbiome" is a hands-on activity designed to demonstrate the dynamics of microbiome ecology. Using pre-prepared bags of their "digestive system microbiome" (Fig. 1), dried pasta, lentils, and a key (Fig. 2), students decipher which foods their microbiome can feed upon and whether there is any habitat space for additional pasta "microbes" to occupy. To model the disturbance event of taking broad spectrum antibiotics on the human digestive system microbiome, students are asked to remove certain "antibiotic sensitive" pasta (Fig. 3) from the bag of pasta for three minutes and place them in a waste cup. Upon reexamining their "digestive system microbiome," they should notice that new habitats have opened and recolonize these habitats with



FIGURE 1. Example of digestive system microbiome of omnivore. Note the presence of a few green and orange lentils and that the smallest pasta falls to the bottom of the bag.

 $@2015 \ Author(s). Published by the American Society for Microbiology. This is an Open Access article distributed under the terms of the Creative Commons Attribution-Noncommercial-NoDerivatives 4.0 International license (https://creativecommons.org/licenses/by-nc-nd/4.0/ and https://creativecommons.org/licenses/by-nc-nd/4.0/ legalcode), which grants the public the nonexclusive right to copy, distribute, or display the published work.$

ESTES: DIGESTIVE SYSTEM MICROBIOME MODELING

either "environmental microbes" (the bean and lentil mix, Fig. 4) or "native microbes" from the waste cup. Students should also determine whether increased diversity of microbes allows for a more or less resilient microbiome community and discuss the implications of robustness. Finally, the students examine their recolonized microbiome for the presence of an opportunistic pathogen, *Clostridium difficile*. Green, toxin-producing, or orange, non toxin-producing, lentils represent *C. difficile*. Students with more than five lentils of either color succumb to *C. difficile*-acquired diarrhea. The class can then discuss methods for resolving the *C. difficile* infection.



FIGURE 2. Key to the pasta types that represent bacteria with the ability to feed on meat, dairy, and plant-based diets.



FIGURE 3. "Antibiotic-sensitive" pasta shapes (yellow and green fusilli, ditalini, macaroni, rotelle, and ziti) that should be removed during the antibiotic treatment portion of the activity.



FIGURE 4. Example of bag of environmental bacteria, including both green and orange lentils.

Detailed instructions are provided in the Supplementary Materials. Materials required are one pre-prepared bag of different pasta shapes and a few lentils (the "digestive microbiome") for every two students. Bags of "environmental bacteria" (dried beans and lentils) and cups for collecting discarded pasta are needed for every four students. Bags take ~ 15 min to make for 40 students. Student and teacher handouts included in the Supplementary Materials provide questions to guide the activity and photographic keys. This activity addresses NSES concepts on Interdependent Relationships in Ecosystems (HS-LS2-6, 2-7,4-6) and Natural Selection and Evolution (HS-LS4-2,4-4,4-5).

Extension

This exercise is easily extendable to discuss different aspects of the microbiome. Students can model antibiotic resistance of resident bacteria after the antibiotic treatment. Using tricolored pasta, label one pasta color as "resistant" and the other two as "sensitive." See how this changes the diversity. Students could also use additional pasta or the discarded pasta in the waste cup of the appropriate color to "regrow" their microbiomes from the "resistant" pasta shapes remaining in their bags.

Examining dietary changes is a second extension. Many different studies see changes in the microbiome when people shift from an animal- and fats-based diet to a plant-based diet (see Teachers Supplemental Materials for references). Students can model this shift in microbiome diversity by removing pasta that represent the animal- or plant based-diets as they decide what diet to eat.

CONCLUSION

This activity has been conducted in a lecture on the human microbiome to 40 students in an undergraduate general microbiology course and approximately 20 faculty. Students enjoyed comparing their "digestive system microbiomes" at different times throughout the activity. The three-minute pasta removal during the disturbance event went well, with students removing enough pasta to create new habitat for their environmental bacterial to colonize. There were groans throughout the classroom when some students "acquired *C. difficile*" and were then suffering from chronic diarrhea. Students seemed to enjoy seeing the differences in the model microbiomes throughout the classroom and the exercise. Faculty response was very positive with one organismal faculty commenting on how well this exercise helped bridge the gap between the macro- and microbiology worlds.

SUPPLEMENTAL MATERIALS

Appendix 1: Modeling the Digestive System Microbiome teacher handout

Appendix 2: Modeling the Digestive System Microbiome student handout

ESTES: DIGESTIVE SYSTEM MICROBIOME MODELING

ACKNOWLEDGMENTS

This exercise was first developed to present to Dr. Betsy Wilson's General Microbiology class at the University of North Carolina in Asheville. Julie Dunning Hotopp,

Hervé Tettelin, Karsten Sieber, Kelly Robinson, Nikhil Kumar, James Munro, Shaun Adkins, David Hearn, and Jean Kneebone provided valuable feedback and suggestions for improving this exercise. The author declares that there are no conflicts of interest.